ACAAI W-31
Monday, November 11
1:00 – 3:00 pm

Dermatology Discussion

Introduction to Common Dermatologic Diseases: Overview from a Dermatology Perspective

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Part 1: Atopic Dermatitis Updates: Dr Peter Lio
- Severe Atopic Dermatitis
- Derm Mimics and Crossovers in Allergy

Part 2: Contact Dermatitis & Hypersensitivity Eruptions: Dr Luz Fonacier
- Dermatitis with Scattered Generalized Distribution
- Systemic Contact Dermatitis to Metals, Balsam of Peru etc.
- Hypersensitivity to Medications
- Pruritus Without a Rash

Part 3: Diagnostics:
- Patch Testing
- Skin Biopsies: Interpretation of skin biopsy report
- Scrapings, Microscopy and Culture
  - KOH prep: Tinea Versicolor & Dermatophyte infections
  - Scabies
  - Bites
  - Tzanck prep: HSV

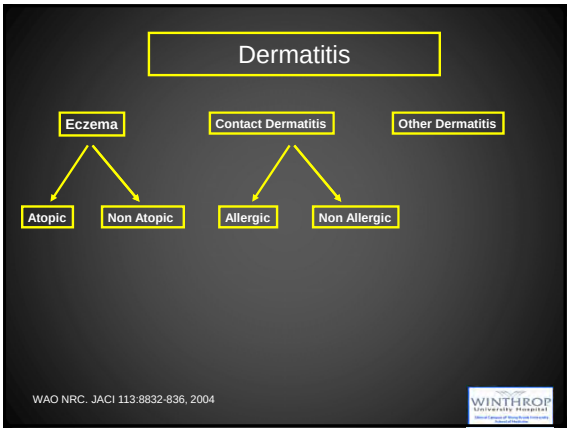
Disclosure

- Research and Educational Grants:
  - Genentec
  - Baxter
  - Merck
  - Dyax
- Speaker's Bureau
  - Baxter

Dermatology Dilemmas:
Objectives:

Upon completion of this workshop, participants should be able to:

1) discuss challenging dermatologic cases in the allergist's office
2) identify the different approaches to disease work-up



WAO NRC. JACI 113:8832-836, 2004

Definition of Eczema

Inflammatory skin reaction
- **Itching**
- **Erythema**
- **Scaling**
- **Clustered papulo-vesicles**

Histology
- **Always present at some stage of eczema:**
  - **spongiosis with acanthosis**
  - **superficial perivascular, lympho-histiocytic infiltrate**

Secondary changes from scratching
- **Excoriations/erosions**
- **Hemorrhage**
- **Lichenification**
- **Secondary infection**

Irritant Contact Dermatitis

Primary diagnostic criteria
- Macular erythema, hyperkeratosis, fissuring with less vesiculation
- Glazed, parched or scalded
- Heal promptly on withdrawal offending agent
- Patch test (-)

Minor objective criteria
- Sharply circumscribed
- Evidence of gravitational influence (dripping effect)
- Less tendency to spread

Rietschel RL, Fowler JF Jr. *Fisher's Contact Dermatitis*. 4th ed. Baltimore, Md: Lippincott Williams & Wilkins; 1995

Comparisons of irritant and allergic contact dermatitis

Criteria	Irritant	Allergic
At risk	Anyone, esp. if repeated exposures	Genetically predisposed & previously sensitized
Mechanism	Direct tissue damage; nonimmunologic	Delayed-type hypersensitivity
Concentration of agent	Usually high; dose effect	May be low; threshold dose; all or nothing
Risk if atopic	Increased	Controversial
Histology	Spongiosis; primarily neutrophilic infiltrates	Spongiosis; primarily lymphocytic infiltrates
Symptoms	Burning, stinging, soreness	Itching
Appearance	Erythema, edema, desquamation, fissures	Erythema, edema, vesicles, papules, lichenification
Demarcation	Usually sharp	Sometimes sharp
Typical onset	Minutes to hours	Hours to days
Common agents	Water, soaps, detergents, acids, bases, solvents, saliva, urine, stool	Poison ivy, poison oak, poison sumac, metals, cosmetics, medicines, foods, rubbers, resins, adhesives

TABLE 3. Body Sites of Dermatitis and Final Diagnoses

Characteristic	Primary, n (%)†	Total of Up to 3 Listed,† n (%)
Dermatitis site	n = 4300*	n = 4308
Scattered/generalized	907 (21.1)	1101 (25.6)
Hand	866 (20.1)	1031 (24.9)
Face	667 (15.5)	926 (21.5)
Eyelids	392 (9.1)	466 (10.8)
Trunk	250 (5.8)	505 (11.7)
Leg	201 (4.7)	469 (10.9)
Arm	184 (4.3)	596 (13.8)
Scalp	150 (3.5)	236 (5.5)
Lips	138 (3.2)	181 (4.2)
Foot	110 (2.6)	263 (6.1)
Anal/Genital	106 (2.5)	134 (3.1)
Other	102 (2.4)	129 (3.0)
Neck	72 (1.7)	366 (8.5)
Most Exposed Areas	62 (1.4)	76 (1.8)
Ears	47 (1.1)	76 (1.8)
Eyes	24 (0.6)	36 (0.8)
Only under clothes	17 (0.4)	27 (0.6)
Nose	3 (0.1)	3 (0.1)
Erythrodermia	2 (0.1)	3 (0.1)

*Excludes 8 with no primary site listed.
†Total of any of up to 3 sites or up to 3 diagnoses listed.
‡Excludes 23 patients with no primary final diagnosis.

Warshaw EM et al. North American Contact Dermatitis Group Patch Test Results for 2009-2010. DERMATITIS. March/April 2013. Vol 24: 2:50-59

Dermatitis with Scattered Generalized Distribution

- Difficult diagnostic & therapeutic challenge: lacks distribution that gives clue to etiology
- Prevalence higher in patients with a history of atopic dermatitis

Dermatitis with Scattered Generalized Distribution

- Allergic Contact Dermatitis with generalized distribution
- Systemic Contact Dermatitis
  - Contact sensitized → exposed orally, transcutaneously, IV or inhalation→ generalized (or localized) dermatitis

SYSTEMIC ALLERGIC CONTACT DERMATITIS

- Reactivation of a previously involved dermatitis
- Reactivation of a previously positive PT
- Baboon Syndrome

Dermatitis with Scattered Generalized Distribution

Two most common allergens:

Nickel

Estimated SCD following oral nickel in nickel allergic patients

- **1% to 0.3 - 0.6 mg/d (normal diet)**
- **10% to 0.55 - 0.89 mg of nickel**
- **~ 50% to 2.5 mg nickel**

Approximate nickel content of foods

- Soybean, ~ 1 cup: 895mcg
- Figs ~5: 85 mcg
- Cocoa, 1 tbsp: 147 mcg
- Lentils ½ cup cooked: 61 mcg
- Cashew, ~ 18 nuts:143 mcg
- Raspberry: 56 mcg
- Vegetables, canned ½ cup: 40 mcg
- Lobster 3 oz: 30 mcg
- Oat Flakes 2/3 cup: 25 mcg
- Peas Frozen, ½ cup: 27 mcg

Balsam of Peru

~ half of patients with (+) PT to MP who followed a low BOP diet had their dermatitis improve

Foods to Avoid in Balsam-Restricted Diet

- Citrus fruits: oranges, lemons
- Flavorings: pastries, bakery goods
- Spices: cinnamon, cloves, vanilla, curry, allspice, anise, ginger
- Spicy condiments: ketchup, chili
- Perfumed or flavored tea & tobacco
- Chocolate
- Ice cream
- Cola, spiced soft drinks
- Tomatoes

Zug KA, Rietschel RL, Warshaw EM, et al. The value of patch testing patients with a scattered generalized distribution of dermatitis: Retrospective cross-sectional analyses of North American Contact Dermatitis Group data, 2001 to 2004. J Am Acad Dermatol 2008;59:426-431

Nickel in Biomedical Devices

Reports of dermatitis to biomedical devices lead to:

- Consultation requests regarding safety of metal medical devices in nickel-sensitized patients
- High variability of care in terms of testing & recommendations
- Increased health care costs
- Medico legal concerns contribute to testing consultations
- Selection of more expensive & less durable option

As nickel allergy incidence increases, this problem also presumably will increase

Komik R and Zug K. Dermatitis2008;19(1):3-8

SUMMARY STATEMENT : The clinician should recognize that contact sensitization to metals or bone cement used in orthopedic, cardiac, other surgical, dental, and gynecological implants have been associated with cutaneous and non-cutaneous presentations (including localized pain, swelling, erythema, warmth, implant loosening, decreased range of motion, or stent stenosis or pericardial effusions in the case of cardiac implants).

Orthopedic Implant Allergy

- 5% of orthopedic implant & up to 21% of patients with preop metal sensitivity may develop cutaneous allergic reactions on reexposure to the same metal
- Clinical manifestations
  - Cutaneous
    - localized: eczematous reaction overlying implant (urticaria & vasculitis reported)
    - generalized
    - both
- Non Cutaneous Reactions
  - Implant Failure

Basko-Plluska JL, Thyssen, JP & Schalock PC. Cutaneous & Systemic Hypersensitivity Reactions to Metallic Implants Dermatitis, 2011;22:65–79
Niki Y, Matsumoto H, Otani T, et al. Screening for symptomatic metal sensitivity: a prospective study of 92 patients undergoing total knee arthroplasty. Biomaterials 2006;26:1019–26

Prospective Longitudinal Studies and Reviews

Study	Pt	Conclusions
Carlsson & Mo¨ller 1989	18	Metal allergic pts with confirmed allergy to metal in their device prior to stainless steel orthopedic implants had no issues (6-yr ff-up)
Thyssen et al, 2009	356	Risk of surgical revision not increased in patients with metal allergies
Niki et al 2006	92	26% had (+) LST tests to at least one metal (Ni, Co, Cr, Fe) 5% of total study developed cutaneous allergic reactions In metal (+) prior to implant: 21% developed dermatitis at site of implant (some widespread)
Eben et al 2010	92	66/92 had sx (pain, reduced motion, swelling) Rates of allergy: nickel: 24.2% vs 3.8% (no Sx); cobalt: 6.1%; vs 3.8% Symptomatic (31.8%) had allergic reaction to bone cement components
Braathen et al	16	81% of failed metal-on-metal implants had metal sensitivity (PT &/or LTT)
Hallab N, et al 2001		Accumulated reports in total hip arthroplasty: prevalence of metal allergy ~ 25% in well-functioning vs. ~ 60% in failed/poorly functioning implant

Carlsson A, Mo¨ller H. Implantation of orthopaedic devices in patients with metal allergy. Acta Derm Venereol 1989;69:62–6.
Thyssen JP, Jakobsen SS, Engkilde K, et al. The association between metal allergy, total hip arthroplasty, and revision. Acta Orthop 2009;80:646–52
Merritt K, Rodrigo JJ. Immune response to synthetic materials.Sensitization of patients receiving orthopaedic implants. Clin Orthop 1996;326:71–9
Niki Y, et al. Screening for symptomatic metal sensitivity: a prospective study of 92 patients undergoing total knee arthroplasty. Biomaterials 2006;26:1019–26.
Eben R et al. Contact allergy to metals and bone cement components in patients with intolerance of arthroplasty. Dtsch Med Wochenschr 2010;135:1418–22.
Thomas P, et al. Increased metal allergy in patients with failed metal-on-metal hip arthroplasty & periimplant T-lymphocytic inflammation. Allergy 2009;64:1157–65
Hallab N, Merritt K, Jacobs JJ. Metal sensitivity in patients with orthopaedic implants. J Bone Joint Surg Am 2001;83:428–36.

Allergic Contact Dermatitis from bone cement components

Reported in 24.8% of patients (n = 239)*

Common Bone Cement Allergen in Total Joint Arthroplasties	Use	Approx % (+) Reaction
N,N-dimethyl-p-toluidine (DPT)	Reaction initiator	10
Polymethyl methacrylate (MMA)	Cement Base	25
Benzoyl Peroxide	Activator	8-10
Hydroquinone	MMA Stabilization	5
Gentamycin	Antibiotic	17-24

Common causes of failure:
infection, recurrent dislocation, aseptic osteolysis, fractures

Thomas P, Schuh A, Eben R, et al. Allergy to bone cement components. Orthopa¨de 2008;37:117–20
Haddad FS, Cobb AG, Bentley G, et al. Hypersensitivity in aseptic loosening of total hip replacements. The role of constituents of bone cement. J Bone Joint Surg Br 1996;78:546–9
Kuehn KD, Ege W, Gopp U. Acrylic bone cements: composition and properties. Orthop Clin North Am 2005;36:17–28

METAL IMPLANT "ALLERGY" Conclusion

- Most reactions to endovascular, orthopedic, dental metal implants are based on case reports or relatively small cohorts
- ~ 5% developed eczematous reactions directly associated with metallic implants
  - proven cases incriminate nickel, cobalt, chromium, copper
- Need for patch testing is controversial, poorly reliable in predicting or confirming implant reaction
  - Preimplantation PT: consider if suspect strong metal allergy
    - Preexisting metal sensitivity with implant containing the offending metal had a higher rate of cutaneous dermatitis
  - Post cutaneous eruption (months - years post implant): PT can be done with an appropriate series of metals

Basko-Plluska JL, Thyssen, JP & Schalock PC. Cutaneous &Systemic Hypersensitivity Reactions to Metallic Implants. Dermatitis, 2011. 22:2: 65–79
*Niki Y, Matsumoto H, Otani T, et al. Screening for symptomatic metal sensitivity: a prospective study of 92 patients undergoing total knee arthroplasty. Biomaterials 2006;26:1019–26.
**Merritt K, Rodrigo JJ. Immune response to synthetic materials. Sensitization of patients receiving orthopaedic implants. Clin Orthop 1996;326:71–9.

METAL IMPLANT "ALLERGY" Conclusion

- (-) PT is reassuring for absence of delayed hypersensitivity
- A (+) PT does not prove relevance
- If relevant allergens are identified & corticosteroid therapy is insufficient to clear eruption, removal of implant may be considered.

Dermatophytide

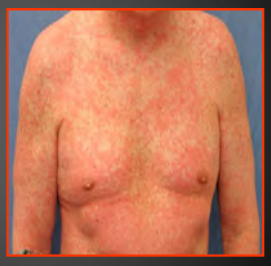
- Secondary distant aseptic lesion
- Criteria
  - Proven focus of dermatophyte infection
  - Positive skin test to group-specific trichophytin antigen
  - Absence of fungi in the id lesion
  - Clearing of id after fungus is eradicated
- Patterns
  - Eczematous vesicles of hands & feet
  - Pityriasis-Rosea like
  - Erysipelas-like
  - Erythroderma

Eczematous Drug Eruption

- Gold: lichenoid features
  - may progress to erythroderma
- Bleomycin
- Penicillin, chloramphenicol
- Quinine
- β-blocker
- Methyldopa
- Clonidine

DRESS Syndrome

- 45 y.o. male
- Started allopurinol 1 week ago
- Fever, malaise, sore throat
- Rash
- Lymphadenopathy
- Shortness of breath
- Increased LFT



Drug Rash with Eosinophilia & Systemic Symptoms
DRESS Syndrome (Drug Hypersensitivity Syndrome)

- Symptoms:
  - Exanthem
  - Fever, malaise, pharyngitis& lymphadenopathy (pseudolymphoma)
  - Involvement of one or more internal organs
    - ~ 50% have hepatitis
    - 30% have eosinophilia
    - 10% have nephritis
    - 10% have pneumonitis
- Usually begin 1 - 8 weeks after exposure
- Tend to persist for some time after drug is stopped

Pruritus without Primary Skin Lesions

- Chronic renal disease
- Cholestasis
- Hematologic disease
  - Iron deficiency
  - Polycythaemia vera
- Endocrine diseases
  - Hypothyroidism Hyperthyroidism
  - Diabetes mellitus
- Malignancy
  - Leukemia
  - Lymphoma
  - Multiple myeloma

*The incidence of generalized pruritus associated with significant internal disease is difficult to assess but is estimated to be ~10%

Pruritus without Primary Skin Lesions

- HIV
- Pregnancy
- Food & drug reactions
- Psychogenic
- Parasitosis
- Idiopathic
- "Wheal-less" urticaria
  - Histamine level & other mediators are sufficient for sensory but not vascular effects
    - Aquagenic pruritus (Kligman AM, Greaves MW. *Arch Dermatol* 1986;24:259-69)
    - Contact urticaria (Kligman AM. *Dermatol Clinic* 1990;8:57-60)
    - Dermographic urticaria (Bernhard JD et al. J *Am Acad Dermatol* 1995;33:322)
    - Cholinergic urticaria (Berth-Jones J. *Br J Dermatol* 1988 121:235-7)

Chronic Renal Disease

- Pruritus is seen in 80% of dialysis patients
- May be localized or generalized, persistent & intractable

Possible pathogenesis of pruritus:

- Dry skin
- Increased non-specific enolase + unmyelinated nerve fibers (Johansson et al, Neurosci Lett 1989;99:281-6)
- Increased PTH from secondary hyperparathyroidism
- Aluminum overload during hemodialysis
  - Treated with desferrioxamine mesylate

Polycythaemia Vera

"Bath itch"

- ~50% of untreated PCV suffer severe, prickly & distressing discomfort within minutes of water contact, lasting 15-60 min
- May precede PCV by several years
- May be associated with elevated serum & urinary histamine levels
- Antihistamines generally ineffective
  - PUVA may be successful

Gilbert HS et al. Blood 1966;28:795-806

Occult Malignancy

- Pruritus is an important but uncommon manifestation of carcinomatosis
- Suspect in the elderly with persistent pruritus
- Solid tumors reported to present with generalized pruritus
  - Adenocarcinomas of lung, colon, breast, uterus, prostate
  - Squamous cell ca
  - Brain tumor: pruritus of nostril

Hodgkin's Disease

- Strongest association of pruritus & malignancy
  - ~30% of patients feel itchy
- Pruritus may be early or presenting symptom
- Intensity may correlate with disease severity
- Itching worse on legs & lower half of body
- Described as burning and more intense at night

Generalized Pruritus That Can Precede Skin Disease

- Bullous Pemphigoid
- Mycosis Fungoides
- Polycythaemia vera
- Hodgkin's Disease

Pruritus of Undetermined Origin (PUO)

Pruritus of > 3 weeks of undetermined origin

- Determining cause of PUO is reported to be 20-30%
- All patients with PUO should be followed up regularly as long as the symptoms persist

Brachioradial Pruritus

- Sunlight induced chronic episodic pruritus localized to outer aspect of elbow & adjacent lower & upper arms
- Commoner in fair-skinned people in tropical climates

- Causes: - probably "solar pruritus"
  - nerve damage from irritation of cutaneous branch of radial nerve or the cervical spine
- Treatment:
  Sun protection, camphor, menthol, cervical spine manipulation, capsaicin, topical anesthetic

Wallcyk PJ *Br J Dermatol* 1986;115:177-80
Bech-Thomjsen N *Acta Derm Venereol (Stockh)* 1995;75:488-9

Part 3: Diagnostics

Patch Testing
Skin Biopsies: Interpretation of skin biopsy report

Scrapings, Microscopy and culture
KOH prep: Tinea Versicolor & Dermatophyte infections
Scabies
Bites
Tzanck prep: HSV

THE TRUE VALUE OF THE T.R.U.E. TEST for the ALLERGIST

	Marks et al. NACDG 1998	Referral Centers Saripelli et al 2003	Derm Private Practice 2006	Allergy Practices 2011 TT 29	Fransway et al NACD 2007-8 TT 36	Warsaw et al NACD 2009-10 TT 36
Clinically relevant allergens by TT	54.1% (completely eval)	25% (completely eval)	~31.7% (at least 1 positive)	56.9% (at least 1 positive)		
Missed positives by TT allergens alone	12.4%	22.4%	~24% (still suspect ACD not in TT)	12.5%	27.2%	26.7%
Additional allergen identified with supplemental PT	34.4%	52.1%		25.6%		

Marks et al.NACDG JAAD 1998;38:911-918
J Am Acad Dermatol 2003;49:65-9.
Militello G et al. Dermatitis, 2006 17;2:77-84
Camacho-Halill M, Axelrod, S,Michels, M, Lighvani, S, Khan, F, Leon, S, Davis-Lorton, M. Aquino M. Fonacier, L. A Multi-center, Retrospective **Review of** Patch Testing For Contact Dermatitis in Allergy Practices. Annals of Allergy, Asthma & Immunology 2011; 107:487-492
Fransway, AF et al. North American Contact Dermatitis Group Patch Test Results for 2007-2008. Dermatitis, , 2013; Vol 24,1 : 10-21
Warshaw EM et al. North American Contact Dermatitis Group Patch Test Results for 2009-2010. DERMATITIS, March/April 2013. Vol 24: 2;50-59

40 Most Frequent (+) reactions to NACG Allergens 2009-2010

		NACD %	T.R..U.E Test
1	Nickel Sulfate	15.5	x
2	Neomycin	8.7	x
3	Fragrance Mix I	8.5	x
4	Bacitracin	8.3	x
5	Balsam of Peru	7.2	x
6	Cobalt Chloride	6.2	x
7	Quarternium 15 (Preservative)	5.8	x
8	Formaldehyde (Preservative)	5.8	x
9	PPD	5.5	x
10	Fragrance Mix II	4.7	
11	Carba Mix	4.6	x
12	Iodopropynyl Butylcarbamate	4.3	
13	Methyl Dibromo-glutaronitrile/phenoxyethanol	3.8	x
14	Popylene Glycol	3.2	
15	Thiuram	3.1	x
16	Colophony	2.7	x
17	Lanolin (Wool Alcohol)	2..5	x
18	MCI/MI	2.5	x
19	Potassium Dichromate	2.3	x
20	Cinnamic Aldehyde	2.3	

al. North American Contact Dermatitis Group Patch Test Results for 2009-2010. DERMATITIS, March/April 2013. Vol 24: 2:50-59

40 Most Frequent (+) reactions to NACG Allergens 2009-2010

		NACD %	T.R.U.E. Test
21	Diazolidinylurea Pet	2.2	x
22	Imidazolidinylurea pet	2.2	x
23	Propolis	2.1	
24	Dimethykaminopropylqmine	2.0	
25	Hydroxyethylnmethacrylate	2.0	
25	Tixocortol Pivalate	2.0	x
27	Compositae Mix	1.9	
28	Benzocaine	1.8	Caine Mix
29	Oleamidopropyl dimethylamine	1.8	
30	Shellac	1.7	
31	Epoxy Resin	1.6	x
32	P-tert-butylphenol Formaldehyde Resin	1.5	x
33	Decyl glucoside	1.5	
34	EthyleneDiamine	1.4	x
35	Cocoamidopropyl betaine	1.4	
36	Manjatole	1.4	
37	Ylang Ylang	1.3	
38	Carvone	1.1	
39	DMDM Hydantoin	1.0	
40	Mixed Diakyl thioureas	1.0	

Frequency of NACD (+) PT in other TRUE Test Allergens

	NACD 2009-10	T.R.U.E. Test
Bromonitropropane	1.0	x
Disperse Blue 106	1.0	x
Paraben mix	0.8	x
Budesonide 0.1% Pet	0.8	x
Mercaptobenzothiazole	0.7	x
Black Rubber mix	0.7	x
Hydrocortisone-17-butyrate	0.7	x
Mercapto mix	0.6	x
Quinolone Mix	NT	x
Caine Mix	(Benzocaine & Dibucaine)	x
Parthenolide	(Sesquiterpene lactone mix & Compositae mix)	x
Gold	NT	x
Thimerosal	NT	x

TRUE TEST vs. NACDG

Of the top 40 NACDG allergens, the following antigens are not on TRUE Test:

- **Fragrance mix II (fragrance) (4.7%)**
- **Iodopropynyl butylcarbamate (preservative) (4.3%)**
- **Propylene glycol (humectant & stabilizer) (3.2%)**
- **Propolis (excipient) (2.1%)**
- **Dimethylaminopropylamine (surfactant) (2.0%)**
- **Hydroxyethyl methacrylate (2.0%)**
- **Oleamidopropyl dimethylamine (surfactant) (1.8%)**
- **Shellac (eye or lip products) (1.7%)**
- **Decyl glucoside (surfactant) (1.5%)**
- **Cocamidopropyl betaine (surfactant) (1.4%)**
- **Majantole (flavoring/fragrance) (1.4%)**
- **ylang ylang oil (flavoring/fragrance) (1.3%)**
- **Carvone (flavoring/fragrance) (1.1%)**
- **DMDM hydantoin (preservative) (1.0%)**
- **Mixed dialkyl thioureas (rubber manufacturing) (1.0%)**

(%) frequency of positive reaction in NACD 2009-2010

Medications, Doses and Patch-Test Results

Pt	Medication	Dose*	Reaction	Allergens	Improved
1	Prednisone	10	+++	Balsam of Peru	Yes
2	Pred + cyclosporine	10 / 200	+++	Cobalt chloride neomycin, Nickel	Yes
3	Cyclosporine	200†	+++	Cobalt chloride Carba mix; thiuram mix; tetraethylthiuram	Yes
4	Infliximab	5‡	+++	n,ndisulfide *-diphenyl-4-phenylenediamine; zinc diethyldithiocarbamate	Yes
5	Prednisone	10	++	p-Phenylenediamine, Disperse Orange 3	Yes
6	Prednisone	10	++	Formaldehyde, Grotan BK, benzalkonium chloride	Yes
7	Cyclosporine	300§	++	Cinnamyl alcohol	Yes
8	Prednisone	10	+	Benzophenone-4, Grotan BK, cocamide DEA, CAPB, oleamidopropyl dimethylamine, Reactive Black 5, dimethylol dihydroxyethyleneurea melamine formaldehyde	No
9	Prednisone	5	+	Euxyl K400, balsam of Peru, nickel oleamidopropyl dimethylamine, carba mix, potassium DC,	No
10	Mycophenolate Off Mycophenolate	2000 -	+ ++ +	Cobalt, gold, triethanolamine Formaldehyde MCI/MI; diazolidinylurea, DMDM hydantoin, melamine formaldehyde	No Yes
11	Prednisone	10	?	Fragrance mix, methyl methacrylate	Yes

? = questionable; aq = aqueous; DEA = diethanolamine; DMDM = dimethylol dimethyl; MCI/MI = methylchloroisothiazolinone/methylisothiazolinone; *All meds (mg/d) continued during PT unless otherwise indicated. †Dcd 2 days prior to testing.‡5 mg/kg/d. Patient on infusion q 8 wks; last dose 3 weeks prior to PT. §Dcd the day of PT.
Rosmarin D, GottliebA et al . Patch-Testing While on Systemic Immunosuppressants. Dermatitis. 20: 05, 265-270 .Oct 2009

PATCH TEST READING

- **Two readings**
  - **1st reading after 48 hours**
  - **2nd reading –3, 4 or 7 days after application**
- **Single reading**
  - **3-4 days after application**
- **1 vs. 2 readings**
  - **2nd reading helps distinguish irritant from allergic responses**
  - **30% of (-) tests at 48 hrs may be (+) on delayed readings**

Delayed Patch Test Reactions after 5 Days

- Metals
  - Gold
  - Potassium Dichromate
  - Nickel
  - Cobalt
- Topical Antibiotics
  - Neomycin
  - Bacitracin
- Topical Corticosteroids
- PPD

Davis M et al. Delayed Patch Test reading after 5 days : the Mayo Clinic Experience. JAAD Aug 2008; 59 (2):225-233

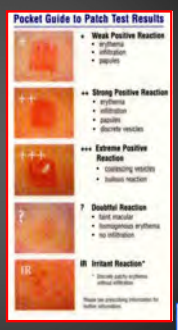
Reactions That Dissipate After Day 5

- Balsam of Peru
- Benzoic Acid
- Disperse Blue #124
- Fragrance mix
- Mercury
- Methylydibromo gluteronitrile/phenoxyethanol
- Natural Fragrance Mix
- Octyl gallate

Davis M et al. Delayed Patch Test reading after 5 days: the Mayo Clinic Experience. JAAD Aug 2008; 59 (2):225-233

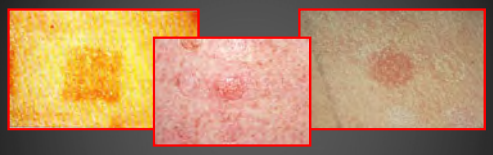
PATCH TEST SCORING

?	Doubtful (faint erythema only)
+	Weak positive (erythema, infiltration, possibly papules)
++	Strong positive (erythema, infiltration, papules, vesicles)
+++	Extreme positive (bullous, ulcerative)
-	Negative
IR	Irritant reaction
NT	Not tested



PATCH TEST INTERPRETATION

➢ ? and + :marginal reactions most difficult to interpret

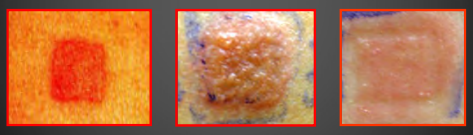


- MAY be allergic if intensity & pruritus develops by 96 hrs
- Common causes: formaldehyde, potassium dichromate, wool wax alcohol, fragrance, paraben, nickel, chlorhexidine, gluteraldehyde
- Clarify by repeat testing or "use test"

Adams.RM.Patch testing-a recapitulation.JAAD.1981;5:629-645

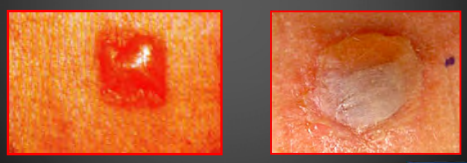
PATCH TEST INTERPRETATION

➢ ++ : consider positive



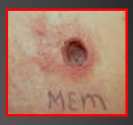
PATCH TEST INTERPRETATION

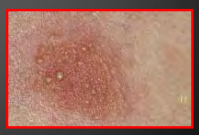
➢ +++: rare, may represent irritant reaction



CAUSES OF FALSE POSITIVE REACTIONS

- Use of irritant substances
  - Sharply demarcate
  - Confined to disc area
  - Shiny, often with blister
  - Burning or painful
  - Decrease severity between readings
- Pustular patch reaction
  - Common in atopics
  - Nickel, copper sulfates, arsenic trioxide & mercuric chloride tests
  - Minimal pruritus





CAUSES OF FALSE POSITIVE REACTIONS

- Angry Back Syndrome: marked ++ to +++ surrounded by +/-or + responses to contiguous site
  - Retest sequentially or at some distance to each other
  - Note multiple true-positives
- Excited Skin Syndrome- more generalized
  - Suspect with >5 reactions
- Negative PT valuable in excluding suspected agent

Relevance

- Present, past, or unknown
- Present relevance further defined
  - Definite
    - Positive use test with suspected item or
    - Positive patch test to product
  - Probable
    - Allergen could be verified as present in known skin contactants and
    - Clinical presentation consistent
  - Possible
    - Patient exposed to circumstances in which skin contact with materials known to contain the allergen likely to occur

TABLE 6. Ten Most Common Sources of Non-NACDG Allergens

Source	No. Patients	Percentage, n = 1022
Cosmetics (personal care products), not otherwise specified	218	21.3%
Clothing	83	8.1%
Moisturizers, lotions	71	6.9%
Jewelry	65	6.3%
Hair dye	37	3.6%
Adhesives, glues, bonding agents	27	2.6%
Topical antibiotics	26	2.5%
Food products	20	2.0%
Perfumes, fragrances	20	2.0%
Lipstick	19	1.9%

Multiple Sensitivity

- Combinations
  - Nickel sulfate/PPD/Benzocaine
    - PPD and Benzocaine cross sensitize
  - Thiuram mix/carba mix/mercapto mix
    - All in rubber, cross sensitization & concomitant sensitization
  - Formaldehyde/Quartenium 15
    - Quartenium 15 is a formaldehyde releaser
  - Paraben, quarternium-15 & formaldehyde: preservatives frequently combined & cosensitize
  - Cobalt & nickel
    - Co-sensitization (cobalt used in alloys with nickel & chromium)
  - Cobalt & potassium dichromate
- Patients > 40y.o. are prone to multiple sensitivities
- Potential involvement of genetic predisposition to chemicals

Dickel H et al. Multiple PT reactions: a pilot evaluation of combination to visualize patterns of multiple sensitivity in PT database Proposal for a multiple sensitivity index. Dermatitis 2003; 14:148-153
Holtzman NA, Marteau TM. Will genetics revolutionize medicine? NEJM 2000;343:141-144
Albert MR et al. Concomitant positive reactions to allergens in the patch testing standard from 1988-1997. Am J Contact Dermat 1999. 10:219-223

CAUSES OF FALSE NEGATIVE REACTIONS

- Insufficient reproduction of conditions of original dermatitis
  - Shoes & clothing - sweating & friction
  - Topical medications - inadequate penetration
- Failure to test true antigen
- Low concentration - threshold of reactivity is too close to irritancy
- Improper testing technique: inappropriate vehicle, poor contact
- Failure to perform delayed readings
- Need for photo patch testing
- Corticosteroid treatment
  - Potent topical steroids on test site
  - Systemic steroids in doses of 20 mg /day or less probably do not inhibit strong reactions*

Condie MW,Adams RM: Influence of oral prednisone on patch test reactions to Rhus antigen. Arch Dermatol 1973. 102:540-543

The Negative Patch Test

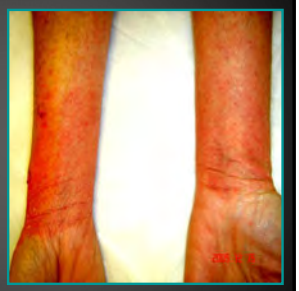
- 34.7% of NACD 2007-2008 had no positive reactions
- Final Classifications:
  - Still ACD : (+) nonstandard allergen in other series, individually tested allergens or patient supplied products
  - Other diagnosis : irritant contact , atopic dermatitis, combination of alternative diagnoses
  - 18.9% given code of "other dermatitis"
    - prognosis in this group is typically poor
    - limited treatment options
    - additional expanded screening series for PT to identify positive relevant allergens
    - Photopatch testing
    - Biopsy and laboratory studies
    - Therapeutic trial

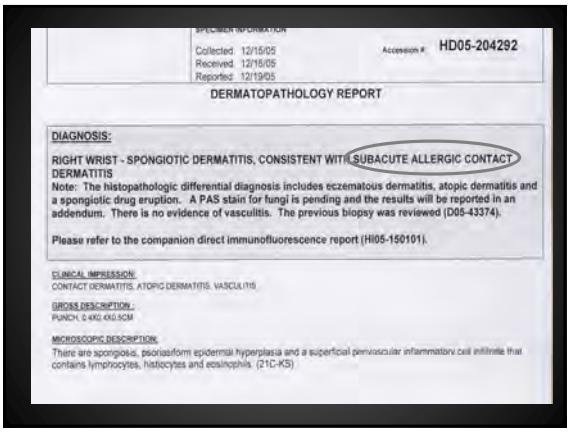
Fransway, AF et al. North American Contact Dermatitis Group Patch Test Results for 2007-2008. Dermatitis, . 2013 Vol 24,1 : 10-21

Terms in Dermatopathology

- **Acantholysis: loss of cohesion between keratinocytes**
- **Acanthosis: Increase number of cells in prickle- cell layer**
- **Hyperkeratosis: increased thickness of stratum corneum**
- **Parakeratosis: retention of keratinocyte nuclei within the horny layer**
- **Spongiosis: intercellular edema**

- 49 y.o female referred by a rheumatologist
- (+) h/o Raynauds, thrombophlebitis, rash
- Extensive workup for SLE, Scleroderma, Dermatomyositis, Mixed Connective Tissue Disease, Anti Phospholipid Syndrome





Collected: 12/15/05
Received: 12/16/05
Reported: 12/19/05
Accession #: HD05-204292

DERMATOPATHOLOGY REPORT

DIAGNOSIS:

RIGHT WRIST - SPONGIOTIC DERMATITIS, CONSISTENT WITH SUBACUTE ALLERGIC CONTACT DERMATITIS
Note: The histopathologic differential diagnosis includes eczematous dermatitis, atopic dermatitis and a spongiotic drug eruption. A PAS stain for fungi is pending and the results will be reported in an addendum. There is no evidence of vasculitis. The previous biopsy was reviewed (D05-43374).

Please refer to the companion direct immunofluorescence report (HI05-150101).

CLINICAL IMPRESSION:
CONTACT DERMATITIS, ATOPIC DERMATITIS, VASCULITIS

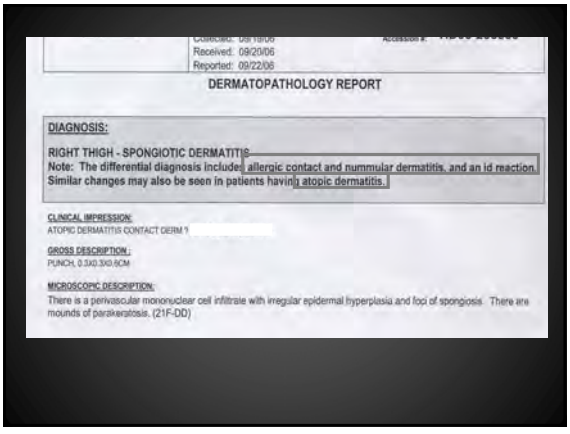
GROSS DESCRIPTION:
PUNCH, 0.4X0.4X0.5CM

MICROSCOPIC DESCRIPTION:
There are spongiosis, psoriasiform epidermal hyperplasia and a superficial perivascular inflammatory cell infiltrate that contains lymphocytes, histiocytes and eosinophils. (21C-K5)

Patch Test

- Positive to
  - 3- (dimethylamino) Propylamine

Cosmetic surfactant used in shampoo, hardener for epoxy resins, additive for dyes, pesticides and binding agents



Received: 09/20/06
Reported: 09/22/06

DERMATOPATHOLOGY REPORT

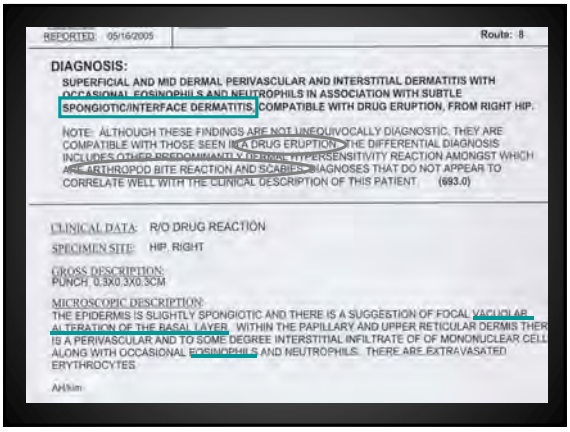
DIAGNOSIS:

RIGHT THIGH - SPONGIOTIC DERMATITIS
Note: The differential diagnosis includes allergic contact and nummular dermatitis, and an id reaction. Similar changes may also be seen in patients having atopic dermatitis.

CLINICAL IMPRESSION:
ATOPIC DERMATITIS CONTACT DERM ?

GROSS DESCRIPTION:
PUNCH, 0.3X0.3X0.6CM

MICROSCOPIC DESCRIPTION:
There is a perivascular mononuclear cell infiltrate with irregular epidermal hyperplasia and foci of spongiosis. There are mounds of parakeratosis. (21F-DD)



REPORTED: 05/16/2005 Route: B

DIAGNOSIS:

SUPERFICIAL AND MID DERMAL PERIVASCULAR AND INTERSTITIAL DERMATITIS WITH OCCASIONAL EOSINOPHILS AND NEUTROPHILS IN ASSOCIATION WITH SUBTLE SPONGIOTIC/INTERFACE DERMATITIS, COMPATIBLE WITH DRUG ERUPTION, FROM RIGHT HIP.

NOTE: ALTHOUGH THESE FINDINGS ARE NOT UNEQUIVOCALLY DIAGNOSTIC, THEY ARE COMPATIBLE WITH THOSE SEEN IN A DRUG ERUPTION. THE DIFFERENTIAL DIAGNOSIS INCLUDES OTHER PREDOMINANTLY DERMAL HYPERSENSITIVITY REACTION AMONGST WHICH ARE ARTHROPOD BITE REACTION AND SCABIES. DIAGNOSES THAT DO NOT APPEAR TO CORRELATE WELL WITH THE CLINICAL DESCRIPTION OF THIS PATIENT. (693.0)

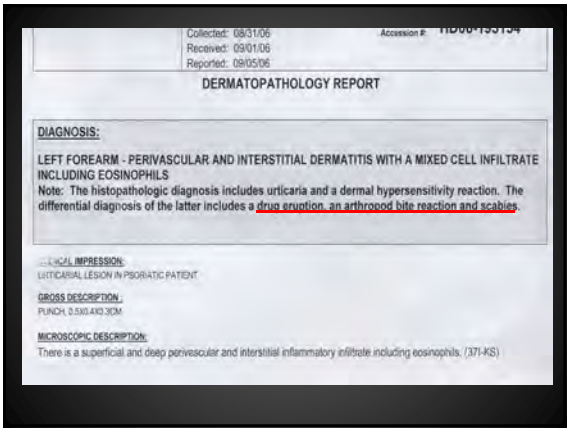
CLINICAL DATA: R/O DRUG REACTION

SPECIMEN SITE: HIP, RIGHT

GROSS DESCRIPTION:
PUNCH, 0.3X0.3X0.3CM

MICROSCOPIC DESCRIPTION:
THE EPIDERMIS IS SLIGHTLY SPONGIOTIC AND THERE IS A SUGGESTION OF FOCAL VACUOLAR ALTERATION OF THE BASAL LAYER. WITHIN THE PAPILLARY AND UPPER RETICULAR DERMIS THERE IS A PERIVASCULAR AND TO SOME DEGREE INTERSTITIAL INFILTRATE OF OF MONONUCLEAR CELLS ALONG WITH OCCASIONAL EOSINOPHILS AND NEUTROPHILS. THERE ARE EXTRAVASATED ERYTHROCYTES.

AH/kim



Collected: 08/31/06
Received: 09/01/06
Reported: 09/05/06
Accession #: HD06-193154

DERMATOPATHOLOGY REPORT

DIAGNOSIS:

LEFT FOREARM - PERIVASCULAR AND INTERSTITIAL DERMATITIS WITH A MIXED CELL INFILTRATE INCLUDING EOSINOPHILS
Note: The histopathologic diagnosis includes urticaria and a dermal hypersensitivity reaction. The differential diagnosis of the latter includes a drug eruption, an arthropod bite reaction and scabies.

CLINICAL IMPRESSION:
URTICARIAL LESION IN PSORIATIC PATIENT

GROSS DESCRIPTION:
PUNCH, 0.5X0.4X0.3CM

MICROSCOPIC DESCRIPTION:
There is a superficial and deep perivascular and interstitial inflammatory infiltrate including eosinophils. (371-KS)

Guidelines for selection of biopsy site

- Ideally a
  - well-developed
  - untreated
  - unscratched lesion
  - representative of the skin disorder
- Old, burnt out lesions with excoriation or lichenification may not reflect primary pathology

Guidelines for Selection of Biopsy Site

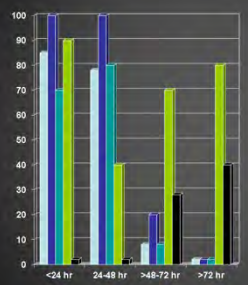
- For blistering diseases
  - Earliest blister if present
  - Erythematous periphery of an unroofed blister

Guidelines for Selection of Biopsy Site

For Vasculitis:

- Edge of new or evolving lesions
- <24 hrs are best
- If fresh lesions are absent, 1/3 from edge of older lesion & 2/3 from adjacent normal to r/o immune complex
- To r/o HSP, take 2nd biopsy of normal skin 10 mm from a lesion

Leukocytoclastic vasculitis



<24 is preferable

>72 hrs yield ~ 40% (-)

Loss of Igs started in <48 hrs

C3 may still be detectable at 48-72 hrs

Duration of Immune Deposits in Cutaneous Vasculitis Lesions by DIF

Adapted from Sais et al. Arch Dermatol 1998:134;309-315